REMARKS/ARGUMENTS

Claims 1-11, 20-24, 26-27 have been withdrawn from consideration pursuant to a restriction requirement. Claims 1-11, 14-24, 26-27 are pending. Claims 14-19 are under consideration.

Citations to the Specification are directed to U.S. Patent Application Publication No. 2005/0215591 (Parthasaradhi et al.).

Favorable reconsideration is respectfully requested in view of the following remarks.

Election

Applicants hereby affirm their prior election with traverse of Group II, reserving their rights under 35 USC § 121 to file a divisional application for the nonelected claims.

Rejection under 35 USC § 103(a)

Claims 14-19 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over WO 97/46527 (Imai). This rejection is respectfully traversed.

The Examiner argues that it is prima facie obvious to pick and choose reacting solvents and conditions to obtain optimum conditions for best yielding of the desired product, and that one in the chemical art is well provided with such skill and the WO 97/46527 provided detailed exemplification in variation of experimental conditions. The Examiner concludes that the picking and choosing of an alternative operating condition consistent with the expectation of optimum product would be produced is prima facie obvious in the chemical art.

However, the claims are patentable over the '527 Imai reference for the following reasons. The framework for the objective analysis for determining obviousness under 35 U.S.C. 103 is stated in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Obviousness is a

question of law based on underlying factual inquiries. The factual inquiries enunciated by the Court are as follows: (A) Determining the scope and content of the prior art; and (B) Ascertaining the differences between the claimed invention and the prior art; and (C) Resolving the level of ordinary skill in the pertinent art. To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385 (CCPA 1970). MPEP 2143.03. It is important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. (*KSR v Teleflex*, 12 S.Ct. 1727, 1740 (US 2007)). Often, it will be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. (*Id.*).

Here, not every element of the claims is taught or suggested in the '527 (Imai) reference. The claims are drawn to a process for the preparation of donepezil hydrochloride monohydrate characterized by an x-ray powder diffraction spectrum having peaks expressed as 2θ at about 5.0, 10.0, 12.7, 13.2, 16.2, 20.0, 21.3, 23.1, 23.9 and 25.3 degrees, which comprises the steps of: a) dissolving donepezil free base in a mixture of chloroform and water; b) adding hydrochloric acid; and c) precipitating donepezil hydrochloride monohydrate from the solution formed in (b) by adding an anti-solvent.

Here, the Examiner has assumed, without providing any evidence, that the methods of

producing donepezil hydrochloride in the '527 Imai reference can be altered to produce the claimed polymorph of donepezil hydrochloride monohydrate.

However, there is no basis for this assumption because the use of different solvents will produce different crystalline forms of a product (see U.S. Patent Application Publication No. 2004/0102523 (Broquaire et al.). Clearly, these are two distinct processes, since the starting donepezil forms are different (i.e. free base vs. salt), and the solvents are different (i.e. chloroform/water vs. methanol). Therefore, the assumption that crystallization from methanol will yield the same polymorphic form as crystallization from chloroform/water has no basis in fact.

In addition, there is no motivation for one of skill in the art to alter the methods of the '527 Imai reference to arrive at the claimed method, and no reasonable expectation of success. There is no teaching or suggestion to alter the method as taught by the '527 Imai reference to arrive at the instantly claimed method. The Examiner argues that one having ordinary skill in the art is well aware of all the pertinent art in the field. The '527 Imai reference discloses dissolving donepezil in methanol, addition of hydrochloric acid, and addition of t-butyl-ether. The '527 Imai reference does not disclose or suggest methods of preparation of donepezil hydrochloride monohydrate crystalline forms by dissolving donepezil free base in chloroform/water. Clearly, these are two distinct processes, since the solvents are different (i.e. chloroform/water vs. methanol). Since the reference does not disclose or suggest this, there is no motivation to employ the process taught by the '527 Imai reference to crystallize donepezil hydrochloride monohydrate and expect to obtain the desired product to reach the limitations of the claims, with the claimed polymorphic form, and no expectation of success.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC § 112 first paragraph

Claims 14-19 stand rejected under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the enablement requirement. This rejection is respectfully traversed.

The Examiner argues that the rejected claims cover making of a product which will display some 2θ peaks using a process ,non-limited in temperature, quantity or ratio of solvents, kind or quantity of anti solvents etc, and that based on the level of skill as stated in the state of the art reference Kirk-Othmer Encyclopedia of Chemical Technology, the amount of guidance in the specification, the disclosure does not contain sufficient information to enable one skilled in the pertinent art for recovery of such a product as claimed, and that state of the art of polymorph recovery is highly unpredictable. The Examiner argues that the Kirk-Othmer article indicates that many uncertain factors determine morphology, and specifically that the appearance of the crystalline product and its processing characteristics (such as washing and filtration) are affected by crystal habit (i.e., the general shape of a crystal).

However, the test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 USC 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971).

Here, the claims are enabled because there is not any reason to doubt the objective truth of the statements contained in the Specification for enabling support. The Specification discloses the manner and process for making and using the claimed invention, including working examples which show the efficacy of the claimed invention. For example, Examples 4 and 5 of the Specification discloses a process of making donepezil hydrochloride monohydrate (see ¶[0053] and ¶[0054]).

Thus, given the teachings of the Specification, in light of the further experimentation carried out by Applicant using the disclosed methods, the quantity of experimentation required is not excessive in view of the subject matter of the claims. The Specification sets forth several methods for producing a monohydrate of donepezil hydrochloride, and the two novel crystalline forms of donepezil hydrochloride monohydrate. Working Examples are also provided, as well as detailed information as to the methods. This information can be used by one of ordinary skill in the art to determine appropriate solution conditions to practice the claimed process, without undue experimentation.

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Rejection under 35 USC § 102(g)

Claims 14-19 are provisionally rejected under 35 U.S.C. 102(g) as allegedly being anticipated by WO 2007/0150052 (Manikowski) which designated the US. This rejection is respectfully traversed.

The Examiner argues that the same monohydrate was disclosed by WO 2007/0150052

and the process of example 21 anticipated the generic claim 14 and rendered the dependent claims obvious since the anti solvent employed in the example is t-bu-methyl ether which is homologous to isopropylether. The Examiner sets forth that Applicants are required to either demarcate the claims from the prior art or provide enabling and factual evidence that the generic claims are reduced to practice by applicants prior to the filing date of the reference.

However, the priority date of the WO 2007/0150052 publication is July 30, 2005. The instant application, U.S. Application No. 10/511,735, is a national stage application under 35 U.S.C. 371 of PCT/IN2003/00158, filing date April 16, 2003. The United States Patent and Trademark Office in its capacity as a Designated / Elected Office (37 CFR 1.495) determined that the international application met the requirements of 35 U.S.C. 371, and was accepted for national patentability examination in the United States Patent and Trademark Office. The filing date of the 10/511,735 application is the international filing date of the international application (Article 11(3) and 35 U.S.C. 363).

Pursuant to 35 U.S.C. 363 an international application designating the United States shall have the effect, from its international filing date under article 11 of the treaty, of a national application for patent regularly filed in the Patent and Trademark Office except as otherwise provided in section 102(e) of this title. Accordingly, the '527 (Imai) reference is not a proper prior art reference under 35 U.S.C. 102(g) over the priority date of the instant application.

In addition, in *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987) (MPEP 2131), the CAFC set forth that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference". In the instant case, not every element of the

claims is present in the '052 (Manikowski) reference. The Examiner argues that the process of example 21 of the '052 (Manikowski) reference anticipates allegedly generic claim 14 and renders the dependent claims obvious since the anti solvent employed in the example is t-bu-methyl ether which is homologous to isopropylether.

However, the claim is drawn to a process for producing a polymorphic form of donepezil hydrochloride monohydrate by dissolving donepezil free base in a mixture of chloroform and water, adding hydrochloric acid, and precipitating donepezil hydrochloride monohydrate from the solution formed by adding an anti-solvent. Therefore, in the claimed process, donepezil free base is mixed in a mixture of chloroform and water, while in contrast the '052 (Manikowski) reference discloses a process in which donepezil hydrochloride (the salt from) is dissolved in methanol.

The use of different solvents will produce different crystalline forms of a product. For example, U.S. Patent Application Publication No. 2004/0102523 (Broquaire et al.) is directed to a process for obtaining crystalline forms of the enantiomers of modafinil, and the crystalline forms which it is possible to obtain according to this process. The '523 publication discloses that "[i]n this method, the nature of the solvent selected and the conditions of crystallization selected can be used to direct the preparation of any of the polymorphic forms. Crystallization solvents and conditions will be disclosed hereinafter for each modafinil form, respectively I, III, IV and VII obtained according to this method" ¶[0109]. Therefore, the assumption that crystallization from methanol will yield the same polymorphic form as crystallization from chloroform/water has no basis in fact. Clearly, these are two distinct processes, since the starting donepezil forms are different (i.e. free base vs. salt), and the solvents are different (i.e. chloroform/water vs.

methanol).

Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

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For at least the reasons set forth above, it is respectfully submitted that the above-identified application is in condition for allowance. Favorable reconsideration and prompt allowance of the claims are respectfully requested.

Should the Examiner believe that anything further is desirable in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicants' undersigned attorney at the telephone number listed below.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
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Please charge or credit our Account No. 03-0075 as necessary to effect entry and/or ensure consideration of this submission.